Amendments to the Drawings:

The attached drawings are black and white replacement drawings for each of the drawings in the application. No other changes to the drawings were made, therefore an annotated sheet is not included.

Attachment: Replacement sheets (Fig. 1-6).

REMARKS

By the present communication, claims 1-4, 7, 10, 13-18, 26 and 33 are amended and claims 36-44 are added. The new claims depend from elected subject matter; therefore, it is requested that they be examined together. Claims 29-35 are withdrawn from consideration. Support for the new and amended claims can be found throughout the application as filed, including, but not limited to paragraphs [0018], [0019], [0021] to [0022], and [0059]. Upon entry of the amendment, claims 1-44 will be pending. In view of the foregoing amendments and the following remarks, Applicant respectfully requests reconsideration of this application.

I. Information Disclosure Statement

The Office Action states that all of the references cited in the Information Disclosure Statement (IDS), filed on 1/5/04 and 9/13/04 have been entered and considered. However, Applicant notes that U.S. Patent No. 6,636,646 on page 1 of the 9/13/04 IDS was not initialed by the Examiner. Accordingly, Applicant respectfully requests that the Examiner consider this reference and initial form PTO-1449 and return a copy to the Applicant.

II. Drawings

The Office Action states that at least one of the drawings is a color drawing or photograph and will not be accepted without a petition. The Examiner did not identify which of the drawings was submitted in color and Applicant has no records indicating which, if any, drawings were submitted in color. Therefore, Applicant is submitting herewith a black and white replacement drawings for each of the drawings in the application.

Applicant believes that the data shown in the figures can be presented in grayscale, without the need for color. Moreover, aspects of the figures which are lost in grayscale reproduction are explained in the text. For Figure 3, paragraph [0084] states that, "Here, colors other than gray scale at $\log 2 \neq 0$ indicate that all 4 measurements consistently show either up-or down-regulation (rule f_0)." For Figure 5, paragraph [0094] provides a reference to a colored rendition in J. Biological Chemistry, Vol. 278, pp. 23830-23833 (2003). In view of the

submission of replacement drawings, Applicant respectfully requests withdrawal of the objection.

III. Specification

The Office Action states that the specification is objected to because of informalities in the title, improper designation of trademarks, and embedded hyperlinks. These informalities have been corrected in the present amendments to the specification. In particular, the title has been amended to: METHODS FOR ELIMINATING INDISTINGUISHABLE AND FALSE DIFFERENTIALS FROM COMPARATIVE DATA MATRICES. Trademark designations for Cy3TM and Cy5TM (paragraph [0047]), SYBR® Green (paragraphs [0039] and [0082]), and Imagene® (paragraph [0092]) have been added. The embedded hyperlink to Trevigen in paragraph [0090] has been removed. Applicant respectfully requests withdrawal of the objections.

IV. Claim Rejections - 35 U.S.C. § 101

Claims 1-28 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter. The Office Action states:

In the instant case, at least one embodiment of the claimed invention merely manipulates data sequences and performs a series of calculations without transforming an article or physical object to a different state or thing outside a computation device.

Furthermore, the invention does not produce a useful, concrete and tangible result. Since the process merely manipulates data sequences and performs a series of calculations, and the process can be performed entirely in a computer or machine or human mind without using or making available for use the results of the manipulation to enable the functionality or usefulness to be realized.

(Office Action, p. 5).

Applicant respectfully traverses the rejection and submits that the claims, as amended, are directed to statutory subject matter. According to the MPEP § 2106,

A claimed invention is directed to a practical application of a 35 U.S.C. 101 judicial exception when it:

(A)"transforms" an article or physical object to a different state or thing; or

(B)otherwise produces a useful, concrete and tangible result, based on the factors discussed below.

Thus, compliance with 35 U.S.C. 101 may be established where a physical transformation occurs or where the claimed invention produces a useful, concrete, and tangible result. A physical transformation is not required for a claimed invention to be directed to statutory subject matter. Rather, compliance with § 101 may be established where the claimed invention produces a useful, concrete, and tangible result. The Federal Circuit has recognized that the transformation of data can produce a useful, concrete, and tangible result. State Street Bank & Trust Co. v. Signature Financial Group Inc., 149 F.3d 1368, 1373 (Fed. Cir. 1998). ("the transformation of data, representing discrete dollar amounts, by a machine through a series of mathematical calculations into a final share price, constitutes a practical application of a mathematical algorithm, formula, or calculation, because it produces 'a useful, concrete and tangible result' - a final share price momentarily fixed for recording and reporting purposes and even accepted and relied upon by regulatory authorities and in subsequent trades."). The process claimed in the pending claims produces a useful, concrete, and tangible result.

MPEP § 2106 states that for an invention to be "useful" it must satisfy the utility requirement of section 101. Claims 1-28 are directed to a practical application which produces a real-world result. MPEP § 2107.01(I). Claim 1 recites method for eliminating indistinguishable differentials from a direct comparison of a pair of samples. The specification states that indistinguishable differentials come from at least two sources:

The first source of unreliable data stems from data points that are indistinguishable from random background noise level of the experimental system. The second source of unreliable data comes from data points that lie above the background noise level, but that are substantially indistinguishable from their corresponding data points in a symmetrical matrix. (Specification, paragraph [0017], emphasis added).

Thus, removing the indistinguishable differentials produces a data set that is more reliable and less likely to be misleading or cause serious errors. The result is a more accurate comparison of the measured properties of two samples. Accordingly, the method of claim 1 and claims 2-28, which depend therefrom, produce a practical, "real-world" result, and therefore satisfy the utility requirement.

MPEP § 2106 states that the "tangible requirement does require that the claim must recite more than a 35 U.S.C. 101 judicial exception, in that the process claim must set forth a practical application of that judicial exception to produce a real-world result." MPEP § 2106 further states that "[i]t is for the discovery or invention of some practical method or means of producing a beneficial result or effect, that a patent is granted" Such practical method and means of producing a beneficial result is reflected in independent claim 1. Specifically, the practical application set forth in claim 1 is the comparison of a measured property of two samples for the purpose of identifying differences between the measured property in the first sample and the measured property in the second sample. The beneficial, real-world result is the elimination of indistinguishable differentials from data generated from the comparison of the two samples which results in the removal of unreliable data, providing a more reliable comparison. The present methods may be used by, for example, persons performing gene expression analysis, protein expression profiling, nucleic acid sequence profiling, or analyzing oligochip data, seismic data, chromatographic data, thermal gravimetric data, and economic data. (See generally paragraphs [0018] and [0025]-[0028]). As stated in MPEP § 2106, "the opposite meaning of "tangible" is "abstract."" A data set which is not misleading and does not contain serious errors is more reliable and therefore beneficial. Thus, there is nothing abstract as to the useful results

produced by the method of claims 1-28. Consequently, claims 1-28 recite tangible subject matter.

With reference to the concrete requirement, MPEP § 2106 states that "[u]sually, this question arises when a result cannot be assured. In other words, the process must have a result that can be substantially repeatable or the process must substantially produce the same result again." MPEP § 2106 goes on to state that the "opposite of "concrete" is unrepeatable or unpredictable." Here, claim 1 recites a method comprising that results in "eliminating indistinguishable differentials from a direct comparison of the pair of samples." It is beyond reasonable dispute that "eliminating indistinguishable differentials" is a result which can be assured. Further, the ranking and curve-fitting steps used to eliminate the indistinguishable differentials are based on the intensity values which once received, do not change. Therefore, the elimination of indistinguishable differentials is both repeatable and predictable for a given data set. For at least these reasons, Applicants respectfully submit that independent claims 1 and claims 2-28 depending therefrom recite concrete subject matter.

Applicant further notes that dependent claims 13-17 and 26-28 are further limited to very specific practical applications, such as a comparison of biomolecule production between biological samples (claim 13 and 14) or comparisons of gene, protein or nucleic acid expression profiles (claims 15-17 and 26-28). The elimination of indistinguishable differentials from a comparison of such biological systems is clearly useful, concrete and tangible. Thus, the Examiner's rejection of these claims is particularly unjustified.

Similarly, new claims 36-44 each set forth a practical application for a specified sample or measured property. For example, claims 36-39 set forth a comparison of the properties of various biological or chemical samples. While claims 40-44 sets forth a comparison between the seismic (claim 40), economic (claim 41), thermal gravimetric (claim 42), chemical or biological (claim 43) or structural, compositional or dynamic properties (claims 44) of a pair of samples. The elimination of indistinguishable differentials from a comparison of any of these systems is

clearly useful, concrete and tangible. Therefore, new claims 36-44 satisfy the requirements of 35 U.S.C. § 101.

Accordingly, Applicants respectfully submit that claims 1-28, as amended, satisfy the requirements of 35 U.S.C. § 101, and request that the Examiner withdraw this rejection.

V. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 1-28 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that "it is unclear what is meant by indistinguishable differentials and it is not clear from what the differentials are indistinguishable." Applicant respectfully traverses the rejection and submits that the term "indistinguishable differentials," viewed in light of the specification, is clear and adequately defined. The specification states that indistinguishable differentials come from at least two sources: data points indistinguishable from background and data points indistinguishable from their corresponding data points in a symmetrical matrix (Specification, paragraph [0017], quoted above). Furthermore, claim 1 has been amended to make clear that steps (a) through (g) of the method are directed toward "eliminating indistinguishable differentials from a direct comparison of the pair of samples." Accordingly, Applicant respectfully requests withdrawal of the rejection. More specifically, claim 1 has been amended to make is clear that the elimination of data points in steps (f) and (g) equate to the elimination of indistinguishable differentials.

Claim 1 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that "ranking the data points from highest to lowest according to intensity" is unclear. Applicant respectfully traverses the rejection, and submits that claim 1, as amended, is clear as to the meaning of intensity. Claim 1 recites that "each data point has an intensity value corresponding to the measured property of the sample." Moreover, in accordance with

Applicant's disclosure, intensity refers to "the value of a given data point of any type." See specification, paragraph [0019]. Thus, it is clear that the "intensity value" for a given data point refers to the value of a measured property of a sample. By way of illustration only, an intensity value may correspond to the level of interaction between a biological sample and an indicator molecule. (See paragraph 34 of the specification.) Accordingly, Applicant submits that the meaning of intensity is clear and requests withdrawal of this rejection.

Claim 1 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that the phrase "on the model curve" lacks clear antecedent basis. Claim has been amended to recite "each of the model curves," thereby correcting the lack of antecedent basis. Likewise, claims 2, 3, and 4 have been similarly amended. With respect to claims 5 and 6, Applicant respectfully traverses the rejection. These claims refer to either one or the other of the model curves generated in step (d) of claim 1. Accordingly, the phrase "model curves" has antecedent basis in claims 5 and 6. Applicant requests withdrawal of this rejection.

Claim 2 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that the variables "C" and "CR" are not defined. Amended claim 2 now defines C as a "constant." See specification, paragraph [0059]. The term "CR" is replaced with the more descriptive phrase "cutoff rank." *See* specification, paragraph [0060]. Accordingly, Applicant requests withdrawal of this rejection.

Claim 7 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that it is unclear how the variables " a_1, \ldots, a_{19} " are defined. Claim 7 has now been amended to state that " (a_1, \ldots, a_{19}) are variables that vary between the model curves." Accordingly, Applicant requests withdrawal of this rejection.

Claim 7 stands rejected under 35 U.S.C. § 112, second paragraph. The Office Action states that the phrase "in the data matrix" lacks clear antecedent basis "because there is prior reference to at least two data matrices in claim 1 from which claim 7 depends." Claim 7 has been amended to refer to the "highest ranking data point in <u>each</u> data matrix." Accordingly,

claim 7, as amended, has antecedent basis in independent claim 1. Accordingly, Applicant requests withdrawal of this rejection.

Claim 13 stands rejected under 35 U.S.C. § 112, second paragraph, because the phrase "expression levels of biomolecules" is allegedly unclear. The Office Action states that "[i]t is know [sic] nucleic acids can be expressed, i.e. DNA being transcribed, RNA being translated. However, it is unclear how a carbohydrate or fatty acid molecule can be expressed." Applicant has amended claim 13 to refer to "amount of biomolecules" making the rejection moot. Accordingly, Applicant requests withdrawal of this rejection.

Claim 17 stands rejected under 35 U.S.C. § 112, second paragraph, because the phrase "oligonucleotide expression levels" is allegedly unclear. Claim 17 has been amended to refer to "nucleic acid expression levels." As the Examiner points out in the Office Action at p. 6, it is known that nucleic acids can be expressed. Accordingly, Applicant requests withdrawal of this rejection.

Claim 18 stands rejected under 35 U.S.C. § 112, second paragraph for reciting "a method for eliminating false differentials" in the preamble, where it is allegedly unclear what is meant by false differentials. The Office Action goes on to state that "the method steps do not recite such a limitation, and thus it is not clear whether it is required as part of the invention and how it is achieved if it is." Applicant respectfully traverses the rejection. The term "false data," viewed in light of the specification, is clear and adequately defined. The specification states that "false differentials" arise from false data that is "erroneous and irreproducible." *See* Specification, paragraph [0017]. The false data "typically result from experimental aberrations or artifacts that are either undetected or undetectable." Claim 18 has also been amended to make clear that steps (a) through (c) of the method are directed toward "eliminating false differentials from a direct comparison of three or more replicate data matrix pairs." More specifically, claim 18 has been amended to make is clear that the elimination of data points in step (c) equates to the elimination of indistinguishable differentials. Accordingly, Applicant respectfully requests withdrawal of the rejection.

Claim 18 stands rejected under 35 U.S.C. § 112, second paragraph, because it is allegedly unclear what is meant by indistinguishable differentials and it is not clear from what the differentials are indistinguishable. Applicant respectfully traverses the rejection. As stated above, the term "indistinguishable differentials," viewed in light of the specification, is clear and adequately defined. The specification states that indistinguishable differentials come from at least two sources: data points indistinguishable from background and data points indistinguishable from their corresponding data points in a symmetrical matrix (Specification, paragraph [0017], quoted above). Furthermore, claim 1 has been amended to make clear that steps (a) through (g) of the method are directed toward "eliminating indistinguishable differentials from a direct comparison of the pair of samples." More specifically, claim 1 has been amended to make is clear that the elimination of data points in steps (f) and (g) equate to the elimination of indistinguishable differentials. Accordingly, Applicant respectfully requests withdrawal of the rejection.

VI. Conclusion

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date <u>May 29, 2007</u>

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